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FOLEY HO	•		LEUNG, JENNIFER A		
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Please find below and/or attached an Office communication concerning this application or proceeding.

Disposition of Claims	•	
Disposition of Claims 4) □ Claim(s) 1-30 is/are pending in the application 4a) Of the above claim(s) is/are withdra 5) □ Claim(s) is/are allowed. 6) □ Claim(s) 1-30 is/are rejected. 7) □ Claim(s) is/are objected to. 8) □ Claim(s) are subject to restriction and/or are subject to restriction and/or are subject to restriction and/or are subject to by the Examination of the drawing(s) filed on is/are: a) □ accomposition and applicant may not request that any objection to the Replacement drawing sheet(s) including the correction and are subjected to by the Examination of the subjection to the Replacement drawing sheet(s) including the correction and are subjected to by the Examination of the subjection to the subjection to the subjection of the subjec	awn from consideration. or election requirement. er. cepted or b) objected to lead on the discontinuity of the	ce. See 37 CFR 1.85(a).
11) The oath or declaration is objected to by the E	•	• • • • • • • • • • • • • • • • • • • •
Priority under 35 U.S.C. § 119		
12) Acknowledgment is made of a claim for foreign a) All b) Some * c) None of: 1. Certified copies of the priority document 2. Certified copies of the priority document 3. Copies of the certified copies of the priority document application from the International Bureat * See the attached detailed Office action for a list	nts have been received. Its have been received in A prity documents have been au (PCT Rule 17.2(a)).	pplication No received in this National Stage
Attachment(s) 1) Notice of References Cited (PTO-892) 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)	4) 🔲 Interview S	ummary (PTO-413))/Mail Date

DETAILED ACTION

Response to Amendment

1. Applicant's amendment submitted on October 25,2004 has been received and carefully considered. Claims 31-58 are cancelled. Claims 1-30 remain active.

Response to Arguments

- 2. Applicant's arguments filed on October 25, 2004 with respect to the rejections of claims 1-30 under 35 U.S.C. 102(b) and/or 103(a) have been fully considered and are persuasive. Therefore, the rejections have been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of the newly applied prior art references, below.
- 3. Applicant's declarations filed on November 26, 2004 have been received and carefully considered. However, the declarations are no longer applicable due to the new grounds of rejection made above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-4, 8, 9, 12-14, 17-19, 22 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kahne (US 5,635,612) in view of Coassin (US 5,405,585).

Regarding claims 1, 2, 12-14, 17-19 and 22, Kahne discloses a process for synthesizing oligosaccharides on a solid phase support (column 29, line 42 to column 32, line 42; column 53, line 25 to column 54, line 8; column 56, lines 15-38), wherein the process comprises the steps of: providing at least one insoluble resin bead (i.e., a support comprising a resin of insoluble polymer that has sites for attaching a glycosyl acceptor via a readily cleavable organic linkage, of which a bead form is well known; column 29, line 44 to column 30, line 23); providing a saccharide donor solution to the reaction vessel (i.e., a glycosyl donor solution comprising a glycosyl sulfoxide; column 31, lines 12-20);

providing an activating reagent solution (i.e., suitable activating agents including, but not limited to, an alkyl- or arylsilyl triflate (e.g., trimethylsilyl triflate), an alkyl- or arylsulfenyl triflate, and an alkyl- or arylselenenyl triflate, of which silyl triflate is a well known equivalent and suitable activating agent; column 31, lines 28-53);

providing a deblocking reagent solution (i.e., for conducting cleavage, or selective removal of protecting groups, via well known processes of debenzylation, acidic hydrolysis of benzylidenes or acetonates, basic hydrolysis of esters, removal of silyl groups with fluoride or under acidic conditions; column 30, lines 6-23; column 32, lines 6-19; column 56, lines 16-24);

providing a solvent (i.e., solvents including, but not limited to, methylene chloride, THF and methanol; column 31, lines 1-11; column 32, lines 6-13); and providing a blocking reagent solution (i.e., for conducting selective addition of protecting

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groups, via well known processes of benzylation, benzylidenation, acetonation, esterification, and carbo- or silylethentication of sugars; column 30, lines 6-23; column 32, lines 6-19; column 56, lines 16-24);

Kahne discloses a suitable apparatus for conducting the process of synthesizing oligosaccharides, wherein the apparatus comprises a reaction vessel for containing the least one insoluble resin bead, the reaction vessel comprising an inlet for the manual addition of solvent and dissolved reagents via canula or syringe needle to the reaction chamber (see FIG. 5A, 5B; column 30, lines 24-68). Kahne further discloses, "[t]here may be many variations on the general apparatus," (column 30, line 30); however, Kahne is silent as to the apparatus further comprising a means for automated delivery of the solvent and dissolved reagents to the reactor chamber, said automated delivery means comprising:

at least one donor vessel for containing the saccharide donor solution; at least one activator vessel for containing the activating reagent solution; at least one deblocking vessel for containing the deblocking reagent solution; at least one solvent vessel for containing the solvent; at least one blocking vessel for containing the blocking reagent solution; a solution transfer system capable of transferring the saccharide donor solution, activating reagent solution, deblocking reagent solution, and solvent to the reaction vessel; and a computer for controlling the solution transfer system.

In any event, it would have been obvious for one of ordinary skill in the art at the time the invention was made to provide such automated delivery means to the apparatus of Kahne, on the basis of suitability for the intended use, because the provision of mechanical or automated means to replace manual activity was held to have been obvious. *In re Venner* 120 USPQ 192 (CCPA 1958); *In re Rundell* 9 USPQ 220 (CCPA 1931). Coassin teaches an automated delivery means

suitable for delivering solvent and reagents to a reactor for conducting solid phase synthesis of oligosaccharides (column 2, line 54 to column 4, line 9), wherein the means comprises a plurality of vessels (i.e., reservoirs 11-21; FIG. 1), each containing an appropriate chemical reagent or solvent for conducting a particular chemical process. The means further comprises a solution transfer system (i.e., comprising tubings 32; valves 41-48) capable of transferring the various reagents or solvents to the reactor vessel (i.e., reactor vessel 50) and a computer for controlling the solution transfer system (i.e., controller 80). The automated delivery means allows for the handling of several types of fluids in a flow system while reducing chemical reagent cross contamination and simplifying system design and control, as taught by Coassin.

Regarding claims 3, 4, 8, 9 and 26, Kahne (FIG. 5A; column 30, lines 62-65; column 31, lines 28-39) discloses a temperature control unit (labeled, "oil bath or cold bath") capable of maintaining the reaction vessel at a temperature of -78 °C. In an example, Kahne further discloses steps of cooling the reaction vessel to temperatures of 0 °C and -60 °C (column 53, line 25 to column 54, line 9). Although the claimed temperature ranges are not recited in the Kahne reference, it would have been obvious for one of ordinary skill in the art at the time the invention was made to select an appropriate temperature for the reaction vessel in the apparatus of Kahne, on the basis of suitability for the intended use, because the temperature control unit is inherently capable of temperature adjustment, as evidenced by the multiple temperatures disclosed above, and furthermore, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art, *In re Aller, 105 USPQ 233*. Additionally, Kahne is silent as to the temperature control unit having its temperature adjustment being controlled by a computer. In any event, it would have been

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obvious for one of ordinary skill in the art at the time the invention was made to provide a computer for controlling the temperature control unit in the modified apparatus of Kahne, on the basis of suitability for the intended use, because the provision of computers to automatically regulate the temperature of temperature control units is well known in the art.

Regarding claims 15 and 16, although Kahne is silent as to the deblocking reagent solution comprising sodium methoxide or hydrazine, it would have been obvious for one of ordinary skill in the art at the time the invention was made to select sodium methoxide or hydrazine for the deblocking reagent solution in the modified apparatus of Kahne, on the basis of suitability for the intended used, because such reagents are well known deblocking reagents in the art.

Regarding claims 23-25, although Kahne is silent as to the blocking reagent solution comprising a benzyl trichloroacetimidate or a carboxylic acid such as levulinic acid, it would have been obvious for one of ordinary skill in the art at the time the invention was made to select a benzyl trichloroacetimidate or a carboxylic acid such as levulinic acid for the blocking reagent solution in the modified apparatus of Kahne, on the basis of suitability for the intended used, because such reagents are well known blocking reagents in the art.

5. Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kahne (US 5,635,612) in view of Coassin (US 5,405,585), as applied to claims 1 and 3 above, and further in view of Lapluye et al. (US 5,466,608).

Regarding claim 5, Kahne is silent as to the temperature control unit comprising a means for measuring the internal temperature of the reactor vessel. Lapluye et al. an apparatus for the synthesis of macromolecules, including oligosaccharides, wherein the internal temperature of a

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reactor 10 is measured by a temperature probe 36 (FIG. 1; column 4, lines 32-47; column 6, line 63 to column 7, line 1). It would have been obvious for one of ordinary skill in the art at the time the invention was made to provide a means for measuring the internal temperature of the reactor vessel in the modified apparatus of Kahne, on the basis of suitability for the intended use, because the means for measuring the internal temperature would allow for a user to monitor the development of an ongoing reaction by detecting variations in temperature to determine the end of the reaction, as taught by Lapluye et al. (column 2, lines 23-43).

Regarding claim 6, Kahne is silent as to whether the reactor and bath structure (FIG. 5A) may comprise a double-wall structure forming two cavities, wherein a first cavity accommodates the synthesis of oligosaccharides and a second cavity accommodates a coolant of the temperature control unit. Lapluye et al. teaches a reactor for the synthesis of macromolecules, including oligosaccharides, wherein the reactor comprises a double-wall structure forming two cavities (i.e., a cylindrical double wall vessel 16 defining an outer cavity for thermoregulated liquid 18 and an inner cavity for accommodating the synthesis of oligosaccharides on resin 12; FIG. 1). It would have been obvious for one of ordinary skill in the art at the time the invention was made to substitute a reactor comprising a double-wall structure for the reactor and bath structure in the modified apparatus of Kahne, on the basis of suitability for the intended use, because the substitution of known equivalent structures involves only ordinary skill in the art. *In re Fout* 213 USPQ 532 (CCPA 1982); *In re Susi* 169 USPQ 423 (CCPA 1971); *In re Siebentritt* 152 USPQ 618 (CCPA 1967); *In re Ruff* 118 USPQ 343 (CCPA 1958).

Regarding claim 7, Lapluye et al. is silent as to the double wall structure 16 of the reaction vessel being comprised of glass. In any event, it would have been obvious for one of

ordinary skill in the art at the time the invention was made to select glass for the material of the double wall structure in the modified apparatus of Kahne, on the basis of suitability for the intended use, because the use glass for reactor materials is well known in the art, since the material is inherently inert to the fluids and reactants.

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6. Claims 10, 11, 20, 21 and 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kahne (US 5,635,612) in view of Coassin (US 5,405,585), as applied to claim 1 above, and further in view of Andrade et al. (Organic Letters, 1999, vol. 1, no. 11, 1811-1814).

Regarding claims 10 and 11, although Kahne is silent as to whether a glycosyl trichloroacetimidate or phosphate may be used for the saccharide donor solution, it would have been obvious for one of ordinary skill in the art at the time the invention was made to select a glycosyl trichloroacetimidate or a glycosyl phosphate for the saccharide donor solution in the modified apparatus of Kahne, on the basis of suitability for the intended use, because the substitution of known equivalent structures involves only ordinary skill in the art. In re Fout 213 USPQ 532 (CCPA 1982); In re Susi 169 USPQ 423 (CCPA 1971); In re Siebentritt 152 USPQ 618 (CCPA 1967); In re Ruff 118 USPQ 343 (CCPA 1958). As evidenced by Andrade et al., glycosyl trichloroacetimidates and phosphates, in addition to the glycosyl sulfoxides as used in the method of Kahne, are well known saccharide donors used for synthesizing oligosaccharides (page 1, column 1, first paragraph, to page 2, column 1, third paragraph).

Regarding claims 20, 21, 27 and 28, although Kahne is silent as to the specifically claimed combination of reagents and solvents, it would have been an obvious design choice for one of ordinary skill in the art at the time the invention was made to an appropriate combination of reagents and solvents well known for the synthesis of oligosaccharides in the modified

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apparatus of Kahne, on the basis of suitability for the desired oligosaccharide structure to be synthesized, in absence of showing any unexpected results thereof.

Regarding claims 29, Kahne is silent as to the insoluble resin bead being comprised of an octenediol functionalized resin. Andrade et al. teach an insoluble resin bead for use in the synthesis of oligosaccharides, wherein the resin bead is comprised of an octenediol functionalized resin (page 2, column 1, third paragraph to column 2, second paragraph). It would have been obvious for one of ordinary skill in the art at the time the invention was made to select an octenediol functionalized resin for the insoluble resin bead in the modified apparatus of Kahne, on the basis of suitability for the intended use, because the resin, when used for the preparation of glycosyl phosphates or trichloroacetimidates, produces high stepwise coupling yields and short reaction times, as taught by Andrade et al.

Regarding claim 30, although Kahne is silent as to whether the organic linker may be comprised of a glycosyl phosphate, it would have been an obvious design choice for one of ordinary skill in the art at the time the invention was made to select a glycosyl phosphate for the organic linker in the modified apparatus of Kahne, on the basis of suitability for synthesizing oligosaccharides from glycosyl phosphate saccharide donors, because such linkers are well known in the art.

7. Claims 1, 2, 10, 12-20 and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Toth et al. (WO 98/08799) in view of Coassin (US 5,405,585).

Regarding claims 1, 2, 10, 12, 14-20 and 22, Toth et al. discloses a process of synthesizing oligosaccharides, wherein the process components are to be provided in an apparatus of "kit" form, wherein the "kit" may include a resin-linker-saccharide support or resin-

linker support and, optionally,

"... one or more further reagents such as protecting agents, deprotecting agents, and/or solvents suitable for solid phase or combinatorial synthesis. The person skilled in the art will be aware of suitable further reagents. Different types of kit can then be chosen according to the desired use." (page 9, line 29 to page 10, line 5).

Thus, it would have been obvious for one of ordinary skill in the art at the time the invention was made to provide a kit comprising:

at least one insoluble resin bead (e.g., a support comprising any resin that swells in water and/or an organic solvent, an organic linker, and a sugar attached to the resin-linker unit such as an unprotected, partially protected or fully protected glycoside; page 10, lines 5-11; page 11, lines 14-18; page 5, line 34 to page 7, line 15; page 14, line 28 to page 15, line 9);

saccharide donor solutions (e.g., a donor solution comprising any activated sugar, including but not limited to trichloroacetimidates; column 11, lines 19-30);

activating reagent solutions (e.g., trimethylsilyl trifluoromethanesulfonate; page 17, lines 5-9), deblocking reagent solutions (e.g., deprotecting agents, hydrazine, sodium methoxide; page 12,

lines 4-16; page 16, lines 12-25; page 17, lines 20-23);

solvents (e.g., dichloromethane, MeOH, THF; page 17, line 8 and line 22; page 18, line 30); and blocking reagent solutions (i.e., protecting agents; page 9, line 37).

As described in Examples 1-52, it appears that the disclosed reagents and solvents of the kit are used to manually synthesize a variety of oligosaccharides (i.e., no mechanical means are disclosed). Thus, Toth et al. is silent as to whether the oligosaccharide synthesis may be automated by conducting the synthesis in an apparatus comprising:

a reaction vessel for containing the at least one insoluble resin bead;

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at least one donor vessel containing the saccharide donor solution;

at least one activator vessel containing the activating reagent solution;

at least one deblocking vessel containing the deblocking reagent solution;

at least one solvent vessel containing the solvent;

a solution transfer system capable of transferring the saccharide donor solution, activating reagent solution, deblocking reagent solution, and solvent to the reaction vessel; and a computer for controlling the solution transfer system.

In any event, it would have been obvious for one of ordinary skill in the art at the time the invention was made to provide means for automating the synthesis of oligosaccharides in the process of Toth et al., on the basis of suitability for the intended use, because the provision of mechanical or automated means to replace manual activity was held to have been obvious. *In re Venner* 120 USPQ 192 (CCPA 1958); *In re Rundell* 9 USPQ 220 (CCPA 1931). Coassin teaches an apparatus suitable for conducting the synthesis of oligosaccharides (column 2, line 54to column 4, line 9), wherein the apparatus comprises a plurality of vessels (i.e., reservoirs 11-21; FIG. 1), each containing an appropriate chemical reagent or solvent for conducting a particular chemical process. The apparatus further comprises a solution transfer system (i.e., comprising tubings 32; valves 41-48) capable of transferring the various reagents or solvents to the reactor vessel (i.e., reactor vessel 50) and a computer for controlling the solution transfer system (i.e., controller 80). The automated apparatus allows for the handling of several types of fluids in a flow system while reducing chemical reagent cross contamination and simplifying system design and control, as taught by Coassin.

Regarding claim 13, althought Toth et al. is silent as to the activating reagent solution comprising silyl trifluoromethanesulfonate, it would have been obvious for one of ordinary skill in the art at the time the invention was made to select silyl trifluoromethanesulfonate for the

activating agent solution in the modified apparatus of Toth et al., on the basis of suitability for the intended use, because the use of such reagent as an activating reagent is well known, and the substitution of known equivalents merely involves routine skill in the art.

Regarding claim 20, although Toth et al. is silent as to the specifically claimed combination of reagents and solvents, Toth et al. discloses a combination of, "... one or more further reagents such as protecting agents, deprotecting agents, and/or solvents suitable for solid phase or combinatorial synthesis. The person skilled in the art will be aware of suitable further reagents. Different types of kit can then be chosen according to the desired use." (page 9, line 29 to page 10, line 5). Thus, it would have been an obvious design choice for one of ordinary skill in the art at the time the invention was made to an appropriate combination of reagents and solvents well known for the synthesis of oligosaccharides in the modified apparatus of Toth et al., on the basis of suitability for the desired oligosaccharide structure to be synthesized, in absence of showing any unexpected results thereof.

Regarding claims 23-25, although Toth et al. is silent as to the blocking reagent solution comprising a benzyl trichloroacetimidate or a carboxylic acid such as levulinic acid, it would have been obvious for one of ordinary skill in the art at the time the invention was made to select a benzyl trichloroacetimidate or a carboxylic acid such as levulinic acid for the blocking reagent solution in the modified apparatus of Toth et al., on the basis of suitability for the intended used, because such reagents are well known blocking reagents in the art.

8. Claims 11, 21, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Toth et al. (WO 98/08799) in view of Coassin (US 5,405,585), as applied to claims 1 and 2 above, and further in view of Andrade et al. (Organic Letters, 1999, vol. 1, no. 11, 1811-1814).

Regarding claim 11, although Toth et al. is silent as to the saccharide donor solution comprising a glycosyl phosphate, Toth et al. discloses that, "The building block mono- or oligosaccharide donors may be any activated sugar, *including but not limited to...*" the various recited saccharide donors (see page 11, lines 19-30). Thus, it would have been obvious for one of ordinary skill in the art at the time the invention was made to select a glycosyl phosphate for the saccharide donor solution in the modified apparatus of Toth et al., on the basis of suitability for the intended use, because the substitution of known equivalents involves only ordinary skill in the art. As evidenced by Andrade et al., glycosyl phosphates, in addition to the trichloroacetimidates used in the method of Toth et al., are well known donors used for synthesizing oligosaccharides (page 1, column 1, first paragraph, to page 2, column 1, third paragraph).

Regarding claim 21, although Toth et al. is silent as to the specifically claimed combination of reagents and solvents, including a glycosyl phosphate donor (see Andrade above), Toth et al. discloses a combination of, "... one or more further reagents such as protecting agents, deprotecting agents, and/or solvents suitable for solid phase or combinatorial synthesis. The person skilled in the art will be aware of suitable further reagents. Different types of kit can then be chosen according to the desired use." (page 9, line 29 to page 10, line 5). Thus, it would have been an obvious design choice for one of ordinary skill in the art at the time the invention was made to an appropriate combination of reagents and solvents well known for the synthesis of oligosaccharides in the modified apparatus of Toth et al., on the basis of suitability for the desired oligosaccharide structure to be synthesized, in absence of showing any unexpected results thereof.

Regarding claims 29, Toth et al. is silent as to the insoluble resin bead being comprised of

an octenediol functionalized resin. Andrade et al. teach an insoluble resin bead for use in the synthesis of oligosaccharides, wherein the resin bead is comprised of an octenediol functionalized resin (page 2, column 1, third paragraph to column 2, second paragraph). It would have been obvious for one of ordinary skill in the art at the time the invention was made to select an octenediol functionalized resin for the insoluble resin bead in the modified apparatus of Toth et al., on the basis of suitability for the intended use, because the resin, when used for the preparation of glycosyl phosphates or trichloroacetimidates, produces high stepwise coupling yields and short reaction times, as taught by Andrade et al.

Regarding claim 30, although Toth et al. is silent as to whether the organic linker may be comprised of a glycosyl phosphate, it would have been an obvious design choice for one of ordinary skill in the art at the time the invention was made to select a glycosyl phosphate for the organic linker in the modified apparatus of Toth et al., on the basis of suitability for synthesizing oligosaccharides from glycosyl phosphate saccharide donors, because such linkers are well known in the art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer A. Leung whose telephone number is (571) 272-1449. The examiner can normally be reached on 8:30 am - 5:30 pm M-F, every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Glenn A. Caldarola can be reached on (571) 272-1444. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent

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system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jennifer A. Leung February 18, 2005

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PRIMARY EXAMINER